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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,531	10/19/2001	Celine Adessi	ADESSI 1	1277

1444 7590 04/19/2004

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EXAMINER	
LU, FRANK WEI MIN	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 04/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/806,531	ADESSI ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2004* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 March 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7/2001* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 1-18 filed on February 2, 2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Therefore, claims 1-18 will be examined. Note that Group II, claims 19, 20, 22-28, 33, and 34 have been canceled by applicant.

Priority

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in European Patent Office on September 30, 1998. It is noted, however, that applicant has not filed a certified copy of this application as required by 35 U.S.C. 119(b).

Specification

3. The disclosure is objected to because of the following informalities: there is no title "BRIEF DESCRIPTION OF THE FRAWINGS" in the specification.

Appropriate correction is required.

Claim Objections

4. Claim 1 is objected to because of the following informalities: (1) "the nucleic acid contains at the 5' end an oligonucleotide sequence Y and at the 3' end an oligonucleotide sequence Z and, the nucleic acid carries at the 5' end a means for attaching the nucleic acid to a

solid support" in step (1) should be "the nucleic acid contains an oligonucleotide sequence Y at the 5' end and an oligonucleotide sequence Z at the 3' end, and the nucleic acid carries a means for attaching the nucleic acid to a solid support at the 5' end"; and (2) "carries at the 5' end a means for attaching the colony primers to a solid support" in step (2) should be "carries a means for attaching the colony primers to a solid support at the 5' end" .

5. Claim 3 is objected to because of the following informality: "step (2)" should be "step (2) of claim 1".

6. Claim 4 is objected to because of the following informalities: (1) "the nucleic acid carries at the 5' end a means for attaching the nucleic acid to a solid support" in step (1) should be "the nucleic acid carries a means for attaching the nucleic acid to a solid support at the 5' end"; and (2) "carries at the 5' end a means for attaching the colony primers to a solid support" in step (2) should be "carries a means for attaching the colony primers to a solid support at the 5' end" .

7. Claims 5, 8, and 16 are objected to because of the following informality: "colonies generated" should be "colonies".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 3 and 5-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claim 3 is rejected as vague and indefinite because it is unclear what means "wherein the sequences of colony primers X are such that the oligonucleotide sequence Z can hybridise to one of the colony primers X and the oligonucleotide sequence Y is the same as one of the colony. primers X". Does this phrase mean that "the oligonucleotide sequence Z can hybridise to one of the colony primers X and the oligonucleotide sequence Y is the same as one of the colony. primers X"? Furthermore, it is unclear that "the sequences of colony primers X" means the sequences of two different colony primers or means the sequences from one of two different colony primers. Please clarify.

11. Claim 5 recites the limitation "the additional step" in the claim. There is insufficient antecedent basis for this limitation in the claim since there is no "an additional step" in claim 1. The examiner suggests applicant to change "the additional step" to "an additional step" in order to overcome the rejection. Please clarify.

12. Claim 5 is rejected as vague and indefinite in view of "the additional step of performing at least one step of sequence determination of one or more of the nucleic acid colonies generated". According to the definition, "nucleic acid colony" is a discrete area comprising multiple copies of a nucleic acid strand (see the specification, page 14, last paragraph), it is unclear how to performing sequence determination of a discrete area comprising multiple copies of a nucleic acid strand. Please clarify.

13. Claim 6 recites the limitation "the incorporation" in the claim. There is insufficient antecedent basis for this limitation in the claim since there is no incorporation step in claims 1 and 5. Please clarify.

14. Claim 6 is rejected as vague and indefinite. Since there is no labeled oligonucleotide in claims 1 and 5, it is unclear how to detect labeled oligonucleotides. Please clarify.

15. Claim 7 recites the limitation "the amplified nucleic acid templates" in the claim. There is insufficient antecedent basis for this limitation in the claim since there is no "amplified nucleic acid templates" in claims 1 and 5. Please clarify.

16. Claim 10 is rejected as vague and indefinite. Since claim 1 does not indicate that a solid support for attaching the nucleic acid and a solid support for the colony primers are identical, it is unclear that "said solid support" recited in claim 10 means a solid support for attaching the nucleic acid or a solid support for the colony primers. Please clarify.

17. Claims 14-18 are rejected because these claims lack antecedent basis since claim 1 does not require a support and all limitations recited in claims 14-18 are dependent on a support recited in claim 1. Please clarify.

Claim Rejections - 35 USC § 102

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an

international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

19. Claims 1-3, 10-12, 14, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Adams *et al.*, (WO 96/04404, published on February 15, 1996).

Adams *et al.*, teach method and apparatus for performing amplification of nucleic acid on supports.

Regarding claims 1 and 10, as shown in Figures 1A to 1M, Adams *et al.*, teach a method for performing amplification (ie., PCR) of nucleic acid on supports. As shown in Figures 1A to 1D, since first nucleic acid 23 is double stranded DNA comprising a first strand 25 and a second strand 27 wherein each strand has two target sequences a and b (see page 14, last paragraph) and second nucleic acid 13 is complementary to a of the first strand 25 and serves as a primer (see page 14, last paragraph bridging to page 15, first paragraph), and has a 5' amino group that is covalently bonded to a latex bead (see page 38, claim 4), the terminus of the second nucleic acid 13 that is close to the latex bead is 5' end and the terminus of the first strand 25 that is close to the latex bead is 3' end. Thus the first strand 25 and the second strand 27 are negative strand (a to b is 3' to 5') and positive strand (a to b is 5' to 3') of the first nucleic acid 23 respectively. Since the first nucleic acid is a fragment of a larger nucleic acid sonicated to produce an approximate length of l kb (see page 23, fourth paragraph), Adams *et al.*, disclose forming at least one nucleic acid template comprising a nucleic acid to be amplified (ie., the first nucleic acid 23 taught by Adams *et al.*,) wherein the nucleic acid contains an oligonucleotide sequence Y at the 5' end (ie., a of the second strand 27) and an oligonucleotide sequence Z at the 3' end (ie., a of the first strand 25) (see attached Figures 1A to 1D with the examiner's handwritings) as recited in step (1) of claim 1. Since 5' end of the first nucleic acid 23 is phosphate, which is

capable to covalently attach to a solid support coated with appropriate chemical groups, Adams *et al.*, disclose that the nucleic acid (ie., the first nucleic acid 23 taught by Adams *et al.*,) carries at the 5' end a means (ie., b of the first strand 25) for attaching the nucleic acid to a solid support as recited in step (1) of claim 1 wherein the means for attaching the nucleic acid template to the solid support comprises a means for attaching the nucleic acid sequences covalently to the said support as recited in claim 10. Since the second nucleic acid 13 is immobilized on a latex bead via amino group at 5' end and hybridizes to a of the first strand 25 (see attached Figures 1A to 1D with the examiner's handwritings and page 23, last paragraph), Adams *et al.*, disclose mixing the at least one nucleic acid template (ie., the first nucleic acid 23 taught by Adams *et al.*,) with one or more colony primers X (ie., the second nucleic acid 13), which can hybridize to the oligonucleotide sequence Z (ie., the second nucleic acid 13) as recited in step (2) of claim 1 wherein the means for attaching the colony primers to the solid support comprises a means for attaching the nucleic acid sequences (ie., amino group at the 5' end) covalently to the said support as recited in claim 10. Since 5' end of the first nucleic acid 23 and the second nucleic acid 13 are capable to attach to a support and claim 1 does not require a support (see above), Adams *et al.*, disclose that one or more colony primers X (ie., the second nucleic acid 13) carries a means for attaching the colony primers to a solid support at the 5' end, in the presence of a solid support, so that the 5' ends of both the at least one nucleic acid template (ie., the first nucleic acid 23 taught by Adams *et al.*,) and the colony primers bind to the solid support as recited in step (2) of claim 1. As shown in Figures 1A to 1M, since, after the amplification, the latex beads have multiple copies of a nucleic acid strand (ie., amplification products 31 and 33) (e.g., see page 16), according to the definition of "nucleic acid colony" (see the specification,

page 14, last paragraph), Adams *et al.*, disclose performing one or more nucleic acid amplification reactions on the bound template (ie., the first nucleic acid 23 taught by Adams *et al.*,) so that nucleic acid colonies are generated as recited in step (3) of claim 1.

Regarding claim 2, since, in the first nucleic acid taught by Adams *et al.*, a of the second strand 27 is an oligonucleotide sequence Y at the 5' end while a of the first strand 25 is an oligonucleotide sequence Z at the 3' end (see above), and a of the second strand 27 or the second nucleic acid 13 is complementary to a of the first strand 25 (see attached Figures 1A to 1D with the examiner's handwritings), Adams *et al.*, disclose that the oligonucleotide sequence Z (ie., a of the first strand 25) is complementary to oligonucleotide sequence Y (ie., a of the second strand 27) and colony primer X (ie., the second nucleic acid 13) is of the same sequence as oligonucleotide sequence Y as recited in claim 2.

Regarding claim 3, since, in the first nucleic acid taught by Adams *et al.*, a of the second strand 27 is an oligonucleotide sequence Y at the 5' end while a of the first strand 25 is an oligonucleotide sequence Z at the 3' end (see above), and a of the second strand 27 or the second nucleic acid 13 is complementary to a of the first strand 25, and the third nucleic acid 15 taught by Adams *et al.*, is complementary to b of the second strand 27 (see attached Figures 1A to 1D with the examiner's handwritings and page 15, first paragraph), Adams *et al.*, disclose that two different colony primers X (ie., the second nucleic acid 13 and the third nucleic acid 15) are mixed with the at least one nucleic acid template (ie., the first nucleic acid 23) in step (2) of claim 1 and wherein one of the sequences of colony primers X (ie., the second nucleic acid 13) can hybridize to the oligonucleotide sequence Z (ie., a of the first strand 25) and the

oligonucleotide sequence Y (ie., a of the second strand 27) is the same as one of the colony primers X as recited in claim 3.

Regarding claims 11 and 12, since Adams *et al.*, teach that the second nucleic acid 13 has a 5' amino group (see page 23, last paragraph) and 5' end of the first nucleic acid 23 is phosphate, Adams *et al.*, disclose that said means for attaching the nucleic acid sequences covalently to the solid support is a chemically modifiable functional group (ie., amino group or phosphate group) as recited in claim 11 wherein said chemically modifiable functional group is a phosphate group, a carboxyl or aldehyde moiety, a thiol, a hydroxyl, a dimethoxytrityl (DMT), or an amino group as recited in claim 12.

Regarding claims 14 and 15, since the support is a glass bead (see page 7, first paragraph), claims 14 and 15 are anticipated by Adams *et al.*.

Therefore, Adams *et al.*, (1996) teach all limitations recited in claims 1-3, 10-12, 14, and 15.

20. Claims 1-3, 10-12, 14, 15, and 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Adams *et al.*, (US Patent No. 6,060,288, filed on February 14, 1997).

Adams *et al.*, teach method for performing amplification of nucleic acid on supports.

Regarding claims 1, as shown in Figures 1A to 1M, Adams *et al.*, teach a method for performing amplification (ie., PCR) of nucleic acid on supports. As shown in Figures 1A to 1D, since first nucleic acid 23 is double stranded DNA comprising a first strand 25 and a second strand 27 wherein each strand has two target sequences a and b and second nucleic acid 13 is complementary to a of the first strand 25 and serves as a primer (see column 8, lines 52-65), and

has a 5' amino group that is covalently bonded to a latex bead (see column 22, lines 48-56), the terminus of the second nucleic acid 13 that is close to the latex bead is 5' end and the terminus of the first strand 25 that is close to the latex bead is 3' end. Thus the first strand 25 and the second strand 27 are negative strand (a to b is 3' to 5') and positive strand (a to b is 5' to 3') of the first nucleic acid 23 respectively. Since the first nucleic acid is a fragment of a larger nucleic acid sonicated to produce an approximate length of l kb (see column 22, lines 42-46), Adams *et al.*, disclose forming at least one nucleic acid template comprising a nucleic acid to be amplified (ie., the first nucleic acid 23 taught by Adams *et al.*,) wherein the nucleic acid contains an oligonucleotide sequence Y at the 5' end (ie., a of the second strand 27) and an oligonucleotide sequence Z at the 3' end (ie., a of the first strand 25) (see attached Figures 1A to 1D with the examiner's handwritings) as recited in step (1) of claim 1. Since 5' end of the first nucleic acid 23 is phosphate, which is capable to covalently attach to a solid support coated with appropriate chemical groups, Adams *et al.*, disclose that the nucleic acid (ie., the first nucleic acid 23 taught by Adams *et al.*,) carries at the 5' end a means (ie., b of the first strand 25) for attaching the nucleic acid to a solid support as recited in step (1) of claim 1 wherein the means for attaching the nucleic acid template to the solid support comprises a means for attaching the nucleic acid sequences covalently to the said support as recited in claim 10. Since the second nucleic acid 13 is immobilized on a latex bead via amino group at 5' end and hybridizes to a of the first strand 25 (see attached Figures 1A to 1D with the examiner's handwritings and column 22, lines 48-56), Adams *et al.*, disclose mixing the at least one nucleic acid template (ie., the first nucleic acid 23 taught by Adams *et al.*,) with one or more colony primers X (ie., the second nucleic acid 13), which can hybridize to the oligonucleotide sequence Z (ie., the second nucleic acid 13) as

recited in step (2) of claim 1 wherein the means for attaching the colony primers to the solid support comprises a means for attaching the nucleic acid sequences (ie., amino group at the 5' end) covalently to the said support as recited in claim 10. Since 5' end of the first nucleic acid 23 and the second nucleic acid 13 are capable to attach to a support and claim 1 does not require a support (see above), Adams *et al.*, disclose that one or more colony primers X (ie., the second nucleic acid 13) carries a means for attaching the colony primers to a solid support at the 5' end, in the presence of a solid support, so that the 5' ends of both the at least one nucleic acid template (ie., the first nucleic acid 23 taught by Adams *et al.*,) and the colony primers bind to the solid support as recited in step (2) of claim 1. As shown in Figures 1A to 1M, since, after the amplification, the latex beads have multiple copies of a nucleic acid strand (ie., amplification products 31 and 33) (e.g., see column 9), according to the definition of "nucleic acid colony" (see the specification, page 14, last paragraph), Adams *et al.*, disclose performing one or more nucleic acid amplification reactions on the bound template (ie., the first nucleic acid 23 taught by Adams *et al.*,) so that nucleic acid colonies (ie., multiple amplification products 31 and 33) are generated as recited in step (3) of claim 1.

Regarding claim 2, since, in the first nucleic acid taught by Adams *et al.*, a of the second strand 27 is an oligonucleotide sequence Y at the 5' end while a of the first strand 25 is an oligonucleotide sequence Z at the 3' end (see above) and a of the second strand 27 or the second nucleic acid 13 is complementary to a of the first strand 25 (see attached Figures 1A to 1D with the examiner's handwritings), Adams *et al.*, disclose that the oligonucleotide sequence Z (ie., a of the first strand 25) is complementary to oligonucleotide sequence Y (ie., a of the second strand

27) and colony primer X (ie., the second nucleic acid 13) is of the same sequence as oligonucleotide sequence Y as recited in claim 2.

Regarding claim 3, since, in the first nucleic acid taught by Adams *et al.*, a of the second strand 27 is an oligonucleotide sequence Y at the 5' end while a of the first strand 25 is an oligonucleotide sequence Z at the 3' end (see above) and a of the second strand 27 or the second nucleic acid 13 is complementary to a of the first strand 25, and the third nucleic acid 15 taught by Adams *et al.*, is complementary to b of the second strand 27 (see attached Figures 1A to 1D with the examiner's handwritings and column 8, lines 52-65), Adams *et al.*, disclose that two different colony primers X (ie., the second nucleic acid 13 and the third nucleic acid 15) are mixed with the at least one nucleic acid template (ie., the first nucleic acid) in step (2) and wherein one of the sequences of colony primers X (ie., the second nucleic acid 13) can hybridize to the oligonucleotide sequence Z (ie., a of the first strand 25) and the oligonucleotide sequence Y (ie., a of the second strand 27) is the same as one of the colony primers X.

Regarding claims 11 and 12, since Adams *et al.*, teach that the second nucleic acid 13 has a 5' amino group (see column 22, lines 48-56) and 5' end of the first nucleic acid 23 is phosphate, Adams *et al.*, disclose that said means for attaching the nucleic acid sequences covalently to the solid support is a chemically modifiable functional group (ie., amino group or phosphate group) as recited in claim 11 wherein said chemically modifiable functional group is a phosphate group, a carboxyl or aldehyde moiety, a thiol, a hydroxyl, a dimethoxytrityl (DMT), or an amino group as recited in claim 12.

Regarding claims 14 and 15, since the support is a glass bead (see column 7, lines 41-52), claims 14 and 15 are anticipated by Adams *et al.*.

Regarding claim 17, the density of colony primers X attached to the solid support is at least 1 fmol/mm^2 (see column 27, lines 50-55).

Therefore, Adams *et al.*, (1997) teach all limitations recited in claims 1-3, 10-12, 14, 15, and 17.

Claim Rejections - 35 USC § 103

21. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

22. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Adams *et al.*, (1996) as applied to claims 1-3, 10-12, 14, and 15 above, and further in view of Huang (US Patent No. 5,645,994, filed on June 6, 1995).

The teachings of Adams *et al.*, have been summarized previously, *supra.*

Regarding claim 4, since claim 1 of this instant application teach all limitations of claim 4

except one or more degenerate colony primer X, as shown above and Adams *et al.*, teach all limitations of claim 1 (see above), Adams *et al.*, disclose all limitations of claim 4 except one or more degenerate colony primer X.

Huang teaches the advantages of the universal primers (ie., degenerate colony primer X), which are: (1) identification of a plurality of species from one sample; and (2) that, by analysis of a sufficient number of the individual amplified molecules, substantially all of the species present in the original sample would be detected and identified (see column 5, fourth and fifth paragraphs).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 4 in view of the patents of Adams *et al.*, and Huang. One having ordinary skill in the art would have been motivated to do so because Huang has successfully used one or more universal primers (ie., degenerate colony primer X) in an amplification reaction and use of the universal primers (ie., degenerate colony primer X) in an amplification reaction would permit identification of a plurality of species from one sample, and, by analysis of a sufficient number of the individual amplified molecules, substantially all of the species present in the original sample would be detected and identified (see column 5, fourth and fifth paragraphs). One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to perform a method recited in claim 4 using one or more universal primers (ie., degenerate colony primer X).

23. Claims 5, 6, 8, and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams *et al.,* (1996) as applied to claims 1-3, 10-12, 14, and 15 above, and further in view of Bukh *et al.,* (US Patent No. 5,514,539, published on May 7, 1996).

The teachings of Adams *et al.,* have been summarized previously, *supra.*

Regarding claims 8 and 9, since Adams *et al.,* teach that biotinylated amplification products are detected by analyzing the conversion of a chemiluminescent substrate by a strepavidin-alkaline phosphatase conjugate using X-ray film or a microscopy (see page 25, third paragraph), Adams *et al.,* disclose visualizing the colonies wherein said visualization step involves the use of a labeled nucleic acid probe as recited in claims 8 and 9.

Adams *et al.,* do not disclose to perform an additional sequence determination step as recited in claim 5 wherein the sequence determination step involves the incorporation and detection of labeled oligonucleotides as recited in claim 6.

Bukh *et al.,* teach that the amplification products of PCR are detected either directly or indirectly (see column 17, last paragraph bridging to column 18, first paragraph).

Regarding claims 5 and 6, Bukh *et al.,* teach the direct detection of the amplification products is carried out via labeling of primer pairs. Labels suitable for labeling the primers include radioactive labels, biotin, avidin, enzymes and fluorescent molecules. The labeled amplified PCR products are also detected via direct sequencing of the PCR-products (see column 17, last paragraph bridging to column 18, first paragraph). Thus Bukh *et al.,* disclose to perform an additional sequence determination step as recited in claim 5 wherein the sequence determination step involves the incorporation and detection of labeled oligonucleotides as recited in claim 6.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed an additional sequence determination step as recited in claim 5 wherein the sequence determination step involves the incorporation and detection of labeled oligonucleotides as recited in claim 6 in view of the patents of Adams *et al.*, and Bukh *et al.*. One having ordinary skill in the art would have been motivated to do so because Bukh *et al.*, have successfully detected PCR products via direct sequencing of the PCR-products and the simple replacement of one well known method (i.e., the method taught by Adams *et al.*,) from another well known method (i.e., detection of PCR products via direct sequencing of the PCR-products taught by Bukh *et al..*,) during the process of detecting labeled PCR products would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because the detection method for PCR products taught by Adams *et al.*, and the detection method for PCR products taught by Bukh *et al.*, are functional equivalent methods which are used for the same purpose (see Bukh *et al.*, column 17, last paragraph bridging to column 18, first paragraph).

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06.

24. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Adams *et al.*, (1996) in view of Bukh *et al.*, (1996) as applied to claims 1-3, 5, 6, 8-12, 14, and 15 above, and

further in view of Hildebrand *et al.*, (US Patent No. 6,287,764 B1, priority date: February 11, 1998).

The teachings of Adams *et al.*, and Bukh *et al.*, have been summarized previously, *supra.*

Adams *et al.*, and Bukh *et al.*, do not disclose that the full or partial sequences of the amplified nucleic acid templates present in more than one nucleic acid colony are determined simultaneously as recited in claim 7.

Hildebrand *et al.*, teach simultaneous sequencing of 10 PCR products (see column 11, last paragraph bridging to column 12, first paragraph) (determination of the full or partial sequences of the amplified nucleic acid templates as recited in claim 7).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have simultaneously determined the full or partial sequences of the amplified nucleic acid templates present in more than one nucleic acid colony in view of the patents of Adams *et al.*, Bukh *et al.*, and Hildebrand *et al.*. One having ordinary skill in the art would have been motivated to do so because Hildebrand *et al.*, have successfully simultaneously sequenced 10 PCR products and simultaneously determining the full or partial sequences of the amplified nucleic acid templates present in more than one nucleic acid colony would save time and laboratory cost. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to simultaneously determine the full or partial sequences of the amplified nucleic acid templates present in more than one nucleic acid colony as recited in claim 7.

25. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Adams *et al.*, (1996) as applied to claims 1-3, 10-12, 14, and 15 above, and further in view of Lund *et al.*, (Nucleic Acids Research, 16, 10861-10880, 1988).

The teachings of Adams *et al.*, have been summarized previously, *supra.*

Adams *et al.*, do not disclose that a mean for attaching the nucleic acid at the 5' end of the nucleic acid template is an amino group as recited in claim 13.

Lund *et al.*, teach that 5'-phosphate group or 5' amino group of a nucleic acid is used to attach the nucleic acid to a solid support (see page 10861, abstract).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have made a nucleic acid template with an amino group at its 5' end as recited in claim 13 in view of the prior art of Adams *et al.*, and Lund *et al.*. One having ordinary skill in the art would have been motivated to do so because Lund *et al.*, have successfully attached a nucleic acid with an amino group at its 5' end and a nucleic acid using its 5' phosphate onto a solid support and the simple replacement of a means for attaching the nucleic acid to a solid support (i.e., 5'-phosphate taught by Adams *et al.*,) from another means for attaching the nucleic acid to a solid support (i.e., 5'-amino group taught by Lund *et al.*,) during the process of making a nucleic acid template recited in claim 13 would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because the replacement would not change the method step of claim 13.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their

expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

26. Claims 16 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams *et al.,* (1996) as applied to claims 1-3, 10-12, 14, and 15 above, and further in view of Fodor *et al.,* (US Patent No. 5,800,992, filed on June 25, 1996).

The teachings of Adams *et al.,* have been summarized previously, *supra.*

Adams *et al.,* do not disclose that the density of the nucleic acid colonies is 10,000/mm^2 to 100,000/mm^2 as recited in claim 16 and the density of the nucleic acid templates is 10,000/mm^2 to 100,000/mm^2 as recited in claim 18.

Fodor *et al.,* teach to make a support immobilized with a nucleic aid wherein the density of the nucleic acid templates is 10,000/mm^2 to 100,000/mm^2 (see column 7, last paragraph).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have made a support immobilized with a nucleic aid wherein the density of the nucleic acid templates is 10,000/mm^2 to 100,000/mm^2 as recited in claim 18 and used the nucleic acid in this support to generate the nucleic acid colonies at a density of 10,000/mm^2 to 100,000/mm^2 as recited in claim 16 in view of the patents of Adams *et al.,* and Fodor *et al.*. One having ordinary skill in the art would have been motivated to do so because Fodor *et al.,* have successfully made a support immobilized with a nucleic aid wherein

the density of the nucleic acid templates is 10,000/mm^2 to 100,000/mm^2. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to make a support immobilized with a nucleic aid wherein the density of the nucleic acid templates is 10,000/mm^2 to 100,000/mm^2 as recited in claim 18 and use the nucleic acid in this support to generate the nucleic acid colonies at a density of 10,000/mm^2 to 100,000/mm^2 as recited in claim 16.

Conclusion

27. No claim is allowed.

28. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703)872-9306 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (571)272-0782.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
PSA
April 15, 2004

FRANK LU
PATENT EXAMINER

part of the office action

Fig. 1A

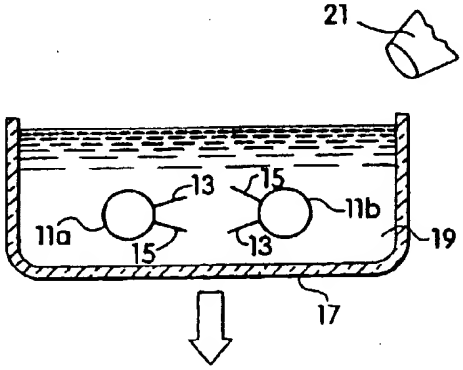


Fig. 1B

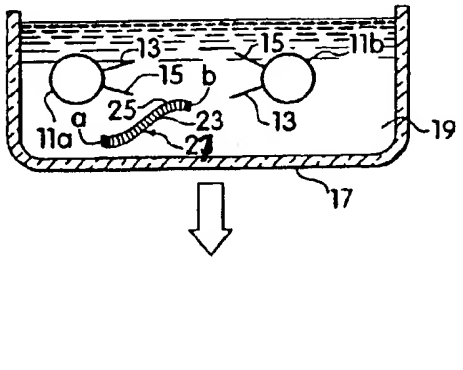
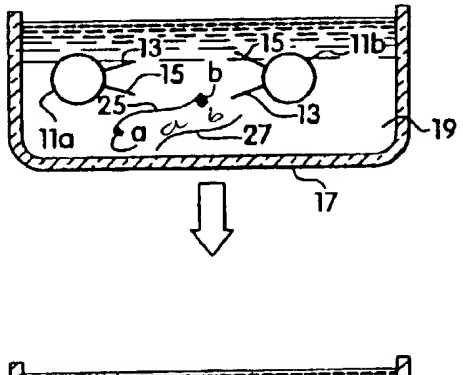


Fig.1C



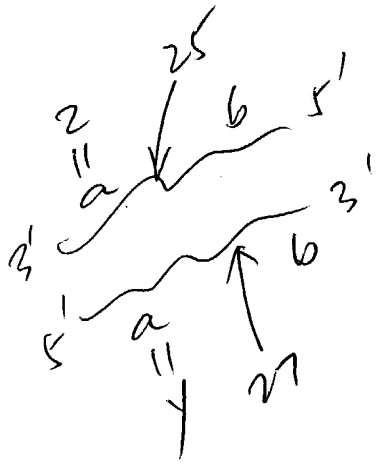
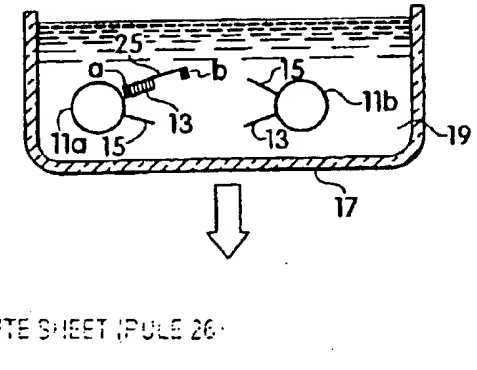


Fig. 1D



part of the office action

Fig. 1A

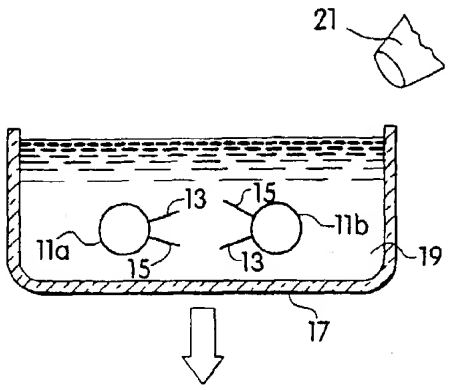


Fig. 1B

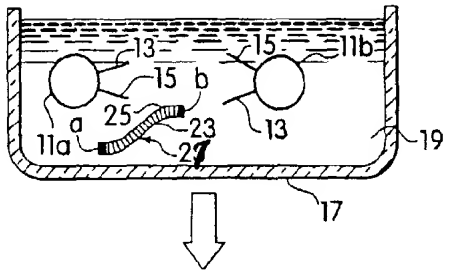


Fig.1C

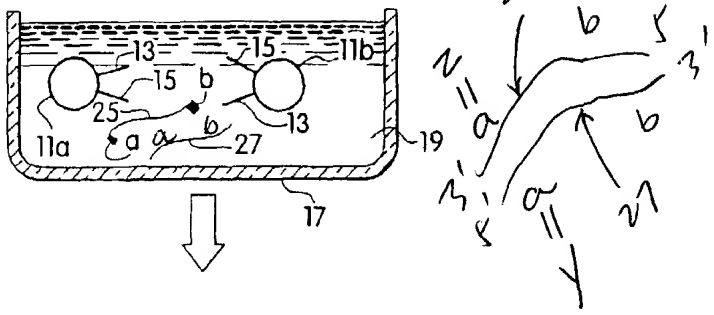


Fig. 1D